

CLAIMS

1. A process for the preparation of L-carnitine inner salt comprising the reduction, with a hydride, of a compound of formula (I)



(I)

where:

X_1 and X_2 , which may be the same or different, are hydroxy, C_1 - C_4 alkoxy, phenoxy, halogen, or X_1 and X_2 , when taken together are an oxygen atom and the resulting compound is a derivative of succinic anhydride;

Y is halogen, the mesyloxy or the tosyloxy group:

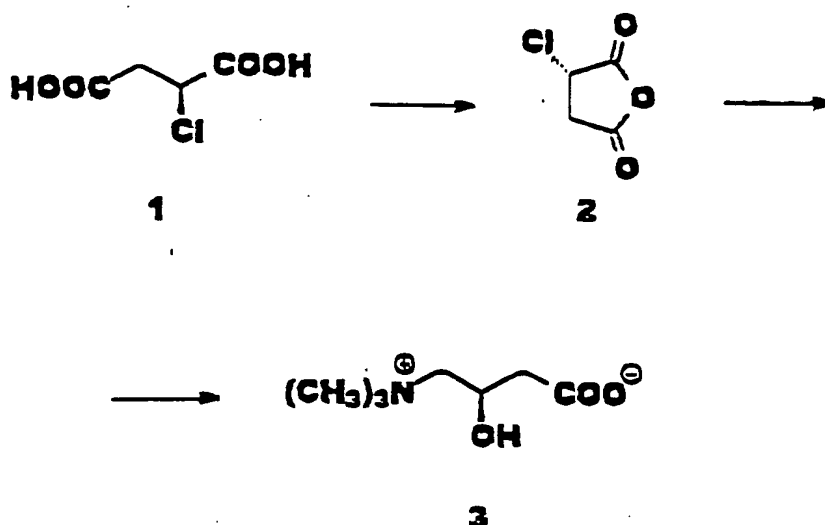
wherein the choice of said hydride will be made in relation to the compound of formula (I) to be treated

and subsequent treatment with a base and then with trimethylamine.

2. A process according to claim 1, in which, in the compound of formula (I), X_1 and X_2 are hydroxy and Y is chlorine, and the reduction is done with diborane.
3. A process according to claim 1, in which, the compound of formula (I), X_1 is hydroxy and X_2 methoxy, Y is halogen, and the reduction is done with lithium borohydride.

4. A process according to claim 1, in which, in the compound of formula (I) , X_1 and X_2 are halogen, Y is halogen, and the reduction is done with sodium borohydride.
5. A process according to claim 1, in which, in the compound of formula (I) , X_1 and X_2 are hydroxy, Y is the mesyloxy group, and the reduction is done with diborane.
6. A process according to claim 1, in which, in the compound of formula (I) , X_1 and X_2 are methoxy, Y is halogen, and the reduction is done with a mixed hydride.
7. A process according to claim 6, in which the reduction is done with lithium borohydride or with lithium and aluminium hydride .
8. 1-methyl hydrogen (S)-2-chlorosuccinate as an intermediate in the process according to claim 1 or 3.
9. (S)-2-clorosuccinoyldichloride as an intermediate in the process according to claim 1 or 4.
10. Use of (S)-methanesulphonyloxysuccinic acid as an intermediate in the process according to claim 1 or 5.
11. A process for the preparation of L-carnitine inner salt according to the following reaction diagram:

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comprising the following steps:

transformation of S-(-)-chlorosuccinic acid into the corresponding S-(-)-chlorosuccinic anhydride;

reduction of S-(-)-chlorosuccinic anhydride with NaBH_4 , in the presence of a solvent, obtaining a compound which, without being isolated, is directly converted to L-carnitine inner salt by treatment with water, then with an alkaline hydroxide and trimethylamine.

12.A process according to claim 11, in which the transformation in step a) occurs with a dehydrating agent.

13.A process according to claim 12, in which said dehydrating agent is selected from the group consisting of acetyl chloride/acetic acid and acetic anhydride, at a temperature ranging from room temperature to 90°C .

14. A process according to claim 11, in which, in step b), the solvent is an aprotic organic solvent or a mixture of organic solvents.

15. A process according to claim 14, in which said aprotic solvent is selected from the group consisting of tetrahydrofuran, monoglyme, diglyme, dioxane, ethyl acetate.

16. S-(-)-chlorosuccinic anhydride as an intermediate in the process of claims 12-15.

17. A process for the preparation of S-(-)-chlorosuccinic acid comprising the reaction between S-(+)-aspartic acid and sodium nitrite in a hydrochloric acid-aqueous milieu being said S-(+)-aspartic acid suspended in demineralised water in a w/v ratio ranging from 1 kg/L to 0.5 kg/L, and concentrated hydrochloric acid being added in a ratio of S-(+)-aspartic acid to hydrochloric acid ranging from 0.35 kg/L to 0.55 kg/L, in the presence of sodium chloride, said S-(+)-aspartic acid and said sodium chloride being in a molar ratio ranging from 1:0.3 to 1:0.5, the improvement wherein consists in the isolation by precipitation of the reaction product by cooling the reaction mixture at a temperature ranging from -10°C to -20°C.

18. A process according to claim 17, in which said temperature is -15°C.

19. A process for the preparation of S-(-)-chlorosuccinic acid comprising the reaction between S-(+)-aspartic acid and sodium nitrite in a hydrochloric acid-aqueous milieu, the improvement wherein consists in using as the reaction medium mother waters from a previous preparation reaction as described in claim 17, said mother waters being used as at least partial substitutes for the sodium chloride and hydrochloric acid envisaged in claim 17.

20. A process according to claim 19, in which said mother waters are used at the precipitation temperature of S-(-)-chlorosuccinic acid envisaged in the process as described in claim 17 or 18.

21. A process according to claim 19 or 20, in which washing waters are used in addition to mother waters.

22. A process according to claim 17, in which the reaction medium comprises washing waters from the process described in claim 19.

23. A process for the preparation of S-(-)-chlorosuccinic acid comprising the reaction between S-(+)-aspartic acid and sodium nitrite in a hydrochloric acid-aqueous milieu, the improvement wherein consists in using as the reaction medium the mother waters of a previous preparation reaction as described in claim 17, said mother waters being transferred to the reactor at the S-(-)-chlorosuccinic acid

precipitation temperature and as at least partial substitutes for the sodium chloride and hydrochloric acid envisaged in claim 17, and said S-(-)-chlorosuccinic acid being isolated by extraction.

5 24.A process for the preparation of S-(-)-chlorosuccinic anhydride which comprises the reaction between S-(-)-chlorosuccinic acid and acetic anhydride, the improvement wherein consists in the use of crude S-(-)-chlorosuccinic acid coming directly from the process described in any of
10 claims 17-22.

25.A process according to claim 17, in which, alternatively, S-(-)-chlorosuccinic acid comes directly from the process described in claim 23.

15 26.A process according to any of the foregoing claims, in which the L-carnitine inner salt is subsequently transformed into one of its salts.

27.A process according to claim 26, in which said salt is a pharmaceutically acceptable salt.